

# Simulation of Heme using DFT+U: a step toward accurate spin-state energetics

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## Abstract

We investigate the DFT+U approach as a viable solution to describe the low-lying states of ligated and unligated iron heme complexes. Besides their central role in organometallic chemistry, these compounds represent a paradigmatic case where LDA, GGA, and common hybrid functionals fail to reproduce the experimental magnetic splittings. In particular, the imidazole pentacoordinated heme is incorrectly described as a triplet by all usual DFT flavors. In this study we show that a U parameter close to 4 eV leads to spin transitions and molecular geometries in quantitative agreement with experiments, and that DFT+U represents an appealing tool in the description of iron porphyrin complexes, at a much reduced cost compared to correlated quantum-chemistry methods. The possibility of obtaining the U parameter from first-principles is explored through a self-consistent linear-response formulation. We find that this approach, which proved to be successful in other iron systems, produces in this case some overestimation with respect to the optimal values of U.

## I. INTRODUCTION

Enzymatic sites containing transition metals are among the most relevant biophysical systems currently studied using first-principles quantum mechanical approaches. The application of such tools, however, is often severely limited as a consequence of the inability of conventional electronic structure methods—such as Hartree-Fock or density-functional theory—to provide a qualitatively correct description of the spin-state energetics of the metal center. Iron porphyrins, which constitute the prosthetic group of the ubiquitous heme proteins, are a paradigmatic example where the aforementioned approaches can not be relied upon to predict the ground state multiplicity of the system.

The spin state of iron porphyrins, as much as the spin state of any transition metal complex, is determined by the coordination symmetry and the nature of the ligands. The three lowest accessible spin states (a singlet, a triplet and a quintuplet if the number of electrons is even, or a doublet, a quartet and a sextet if it is odd) are conventionally referred to as low, intermediate, and high-spin. In unligated porphyrins the metal is coordinated to four in-plane nitrogen atoms, and experimental studies on model compounds, namely on Fe(II) tetraphenylporphine (FeTPP), indicate for this coordination mode a triplet ground state.<sup>1–5</sup> Additional axial ligands produce alternative multiplicities: imidazole gives rise to high spin hemes, while strong ligand-fields as that of diatomic molecules like CO, NO or O<sub>2</sub>, favor low spin configurations.<sup>6</sup> Six coordinated hemes, with two axial ligands, usually exhibit a low spin state unless the ligand-field is extremely weak. Fig. 1 depicts a schematic view of the d-states energy levels in three distinctive coordination environments.

Even though first-principles approaches, specifically Hartree-Fock (HF) and density-functional theory (DFT), greatly contributed to the interpretation and understanding of

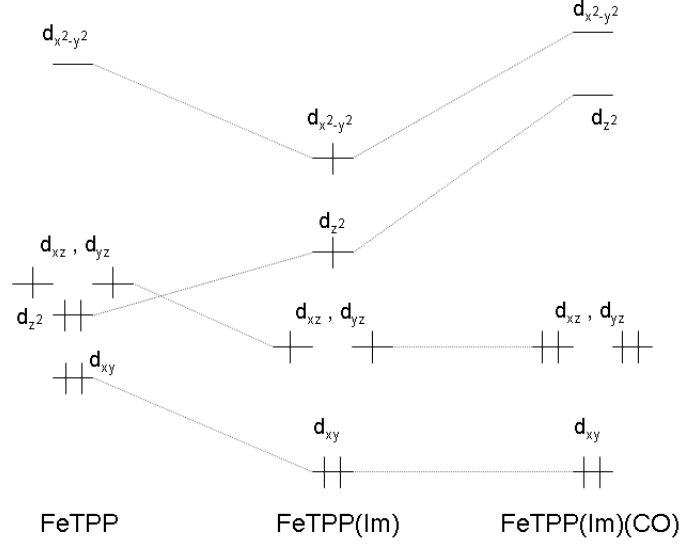


FIG. 1: Schematic representation of the d-orbitals energy levels for FeTPP. From left to right: free (four coordinated), ligated to imidazole (five coordinated), and ligated to imidazole plus CO (six coordinated).

the functional aspects of the active site of heme proteins at the molecular level, attempts to predict the ground state multiplicity of these systems soon made apparent that an accurate description of the electronic structure might require more sophisticated techniques. This fact can be tracked down to the spin-transition energies provided by HF and DFT for isolated iron atoms and ions or different iron compounds, where it has been systematically observed that HF favors high-spin electronic configurations while DFT exhibits a preference for low-spin states.<sup>7–12</sup> Such biases are similarly manifested in heme complexes: Table I summarizes this trend in five and six coordinated iron porphines (FeP).

For the last decade DFT has been the first method of choice to perform electronic structure calculations of biological models, and in particular of heme systems. In this context, one of the most crucial failures of common exchange-correlation functionals has been detected in the deoxygenated active site of hemoglobin and myoglobin (Table I). The earliest

study reporting this flaw is due to Rovira *et al.*,<sup>13</sup> who obtained for the five coordinated model  $\text{Fe}^{\text{II}}\text{P}(\text{Im})$  (axial ligand: imidazole) a triplet state 6.5 kcal/mol below the quintuplet, which is the experimental ground state of the system. After this work, a few others followed which also observed this inversion using B3LYP or different pure GGA functionals.<sup>7,14</sup> Liao and Scheiner claimed to have found a quintuplet ground state for this five coordinated compound employing a DFT-GGA functional.<sup>15</sup> In their calculations, however, electronic symmetry constraints were imposed. To the best of our knowledge, DFT functionals yield for  $\text{Fe}^{\text{II}}\text{P}(\text{Im})$  a triplet ground state in the absence of symmetry constraints. In an effort to quantify the errors in the DFT estimates of spin transition energies, Ghosh and Taylor resorted to highly-correlated techniques as CASPT2 and CCSD(T) to explore the iron (III) porphyrin chloride.<sup>8</sup> This is another example of a high spin five coordinated heme complex for which DFT predicts a quartet favored over the sextet, in this case by around 7 kcal/mol. B3LYP, on the other hand, finds about the same energy for both spin configurations. The more accurate approaches CASPT2 and CCSD(T) agree in yielding a sextet ground state, 16 kcal/mol below the quartet.<sup>8</sup> A latter work by these authors shows the same low-spin bias in B3LYP for the iron (IV) porphyrin difluoride.<sup>9</sup> It is worth noting here that even CASPT2—employed with the moderate active spaces currently affordable—has been found fallible in the estimation of these elusive spin states. Inaccuracies have been reported in the prediction of the electronic ground states of the isolated iron porphyrin<sup>16</sup> and of the oxyheme.<sup>17</sup>

It is possible to find a rationale for the biases in DFT and HF, considering the balance between the computed electronic exchange and correlation energies. In a simplified picture, the (negative) exchange energy is contributed by like spin electron pairs, while electronic correlation arises from the interaction between electrons regardless of their spin. A

method which includes the exchange and neglects the correlation, as HF does, will favor high multiplicities by maximizing the number of electrons with the same spin. To the contrary, experience shows that the combination of the exchange and the correlation terms in pure DFT pushes the balance toward low spin configurations.<sup>12</sup> Attempts to improve the spin state energetics description of density-functionals have mostly been based on hybrid Hartree-Fock/DFT schemes,<sup>7,10,12</sup> which combine the exchange of HF with the exchange and correlation obtained from DFT in proportions obeying empirical considerations. This approach, however, has given no universal functional capable to provide accurate splittings in every case. In general, those functionals offering a good description of the high spin species fail when tried out on low spin complexes, and vice versa.<sup>7</sup> Among them, B3LYP is seemingly the one with the best average performance up to now, yet exhibiting serious inaccuracies in the five coordinated models already discussed.

In the present study, we propose the DFT+U approach as an alternative to the standard ab-initio techniques for a reliable description of the low lying states of iron heme complexes. The LDA+U or GGA+U method (more generally denoted as DFT+U) was originally designed within the density-functional theory framework for the treatment of strongly correlated materials.<sup>18–22</sup> Only very recently researchers have started to apply it to molecular, or mixed solid-molecular systems, with extremely promising results.<sup>23–27</sup> This approach corrects the tendency to overhybridize and delocalize electronic orbitals—ultimately originating in the presence of self-interactions in the exchange-correlation functionals—by introducing a term that penalizes fractional occupancies. We note in passing that in our present implementation we explore the possibility of a  $U$  that is not a best-fit parameter, but an intrinsic, ab-initio linear-response property of the system chosen. However, this approach does not prove totally satisfactory, as in the case of low spin complexes it leads to values of  $U$  lying

1 or 2 eV above the optimal ones. We show that with the inclusion of a single parameter, DFT+U recovers the correct multiplicities of the five coordinated models where DFT and hybrid methodologies are in disagreement with more elaborated techniques or experimental data. Moreover, there is no impairment with respect to GGA functionals in those cases for which DFT displayed the right behavior. Calculations of ligand exchange thermodynamics, spin transitions, and other properties, point to GGA+U as an appealing tool to overcome the limitations entailed by the use of DFT in the description of bioinorganic complexes, at a computational expense much lower than demanded by highly-correlated quantum chemistry methods.

## II. METHODOLOGY

### A. General framework

All calculations reported in this work have been performed with the public domain PWSCF and CP codes included in the Quantum-Espresso distribution,<sup>28</sup> based on density-functional theory, periodic-boundary conditions, plane-wave basis sets, and pseudopotentials to represent the ion-electron interactions. The PBE exchange-correlation functional<sup>29</sup> has been used in combination with Vanderbilt ultrasoft pseudopotentials,<sup>30</sup> with the Kohn-Sham orbitals and charge density expanded in plane waves up to a kinetic energy cutoff of 25 and 200 Ry respectively.

### B. The DFT+U approach

The present implementation of DFT+U stems from the early contributions by Anisimov and others,<sup>18–22</sup> who proposed to correct the failures of the LDA functional in dealing with

the strongly localized d or f electrons of transition metal ions. An on-site correction was thus constructed to account for strong electronic correlations poorly described within the local-density or generalized-gradient approximations, and formulated as follows:

$$E_{DFT+U}[\rho(\mathbf{r})] = E_{DFT}[\rho(\mathbf{r})] + E_U[\{n_{mm'}^{I\sigma}\}] = E_{DFT}[\rho(\mathbf{r})] + E_{HUB}[\{n_{mm'}^{I\sigma}\}] - E_{DC}[\{n^{I\sigma}\}] \quad (1)$$

where  $\rho(\mathbf{r})$  is the electronic density,  $n_{mm'}^{I\sigma}$  are generalized atomic orbital occupations with spin  $\sigma$  associated to the  $I$  atom, and  $n^{I\sigma}$  is the sum of the occupations corresponding to all eigenstates,  $\sum_m n_{mm'}^{I\sigma}$ .  $E_{DFT}[\rho(\mathbf{r})]$  is the standard LDA or GGA energy functional, and  $E_{HUB}[\{n_{mm'}^{I\sigma}\}]$  represents the “correct” on-site correlation energy. Since  $E_{DFT}[\rho(\mathbf{r})]$  already contains an approximate correlation contribution, a term intended to model such a contribution,  $E_{DC}[\{n^{I\sigma}\}]$ , must be subtracted to avoid double counting.

In this work, we resort to the rotationally invariant formulation of DFT+U introduced by Liechtenstein *et al.*<sup>21</sup> and later simplified by Dudarev and his coworkers,<sup>22</sup> in which the non sphericity of the electronic interactions and the differences among the interactions in like-spin and unlike-spin channels are neglected. With these assumptions, the correction to the energy functional can be written

$$E_U[\{n_{mm'}^{I\sigma}\}] = \frac{U}{2} \sum_I \sum_{m,\sigma} [n_{mm}^{I\sigma} - \sum_{m'} n_{mm'}^{I\sigma} n_{m'm}^{I\sigma}] = \frac{U}{2} \sum_{I,\sigma} \text{Tr}[n^{I\sigma}(1 - n^{I\sigma})] \quad (2)$$

where  $U$  is the Hubbard parameter describing on-site correlations. In principle, different definitions for the occupation matrix are possible, which in turn will determine different values for  $U$ . In this case we define

$$n_{mm'}^{I\sigma} = \sum_{\nu} f_{\nu} \langle \psi_{\nu}^{\sigma} | \phi_m^I \rangle \langle \phi_{m'}^I | \psi_{\nu}^{\sigma} \rangle \quad (3)$$

with  $f_{\nu}$  the weight of the electronic state  $\nu$ ,  $\phi_m^I$  the valence atomic orbital  $|lm\rangle$  of atom  $I$ , and  $\psi_{\nu}^{\sigma}$  the one electron wavefunction corresponding to the state  $\nu$  with spin  $\sigma$ . The



diagonalization of the occupation matrices leads to the following expression for the energy correction:

$$E_U[\{n_{mm'}^{I\sigma}\}] = \frac{U}{2} \sum_{I,\sigma} \sum_i \lambda_i^{I\sigma} (1 - \lambda_i^{I\sigma}). \quad (4)$$

Equation (4) clearly reflects the nature of the correction, which imposes a penalty (mediated by  $U$ ) for fractional occupations, thus favoring either fully occupied or empty orbitals ( $\lambda \approx 1$  and  $\lambda \approx 0$ , respectively). We note that under this definition,  $U$  corresponds to the difference  $U - J$  as utilized by Anisimov and other researchers.<sup>20–22</sup> For example, the adoption of  $U=4$  eV in the present calculations is comparable to a  $U$  of 5 eV in combination with a  $J$  of 1 eV in the work of Rollmann.<sup>24</sup> Whereas in recent applications  $U$  is considered a fitting parameter,<sup>24–27</sup> here we obtain it from the spurious curvature of the DFT energy as a function of the occupations. As shown by Cococcioni and de Gironcoli,<sup>31</sup> the value of  $U$  can be estimated as the difference between the screened and bare second derivative of the energy with respect to the occupations:

$$U = \frac{\partial^2 E_{DFT}}{\partial (n^I)^2} - \frac{\partial^2 E_{DFT}^0}{\partial (n^I)^2}. \quad (5)$$

In particular, we are interested in the self-consistent  $U$ , which we will call  $U_{sc}$ , originating from the curvature of the DFT+ $U$  ground state.<sup>23</sup> To compute  $U_{sc}$ , a few linear response calculations must be performed at a finite  $U_{in}$ , each one yielding a corresponding  $U_{out}$ . It can be shown that there is a linear dependence between  $U_{in}$  and  $U_{out}$ , from which  $U_{sc}$  can be extrapolated:<sup>23</sup>

$$U_{out} = \frac{\partial^2 E_{quad}}{\partial (n^I)^2} = U_{sc} - \frac{U_{in}}{m}. \quad (6)$$

$E_{quad}$  groups all electronic terms within the DFT+ $U$  functional that have quadratic dependence on the occupations, whereas  $m$  can be interpreted as an effective degeneracy of the orbitals whose population is perturbed. This procedure, which allowed us to attain

an improved description of the multiplet splittings and bonding in Fe dimers and FeO related species,<sup>23</sup> is the one adopted here to calculate a self-consistent  $U$  parameter for the iron-porphyrin system. Another criterion has also been explored, requesting that a linear response calculation at a finite  $U$  returns this same value of  $U$  at the output, e.g.  $U_{in} = U_{out}$ . The parameter fulfilling this criterion will be hereafter denoted  $U'_{sc}$ . This second criterion is not as appealing as the first one, since  $U_{sc}$  seems the “right definition” for self-consistency.

### III. RESULTS AND DISCUSSION

In this section DFT+U results are presented on four heme complexes:  $\text{Fe}^{\text{II}}\text{P}(\text{Im})$ ,  $\text{Fe}^{\text{III}}\text{P}(\text{Cl})$ ,  $\text{Fe}^{\text{II}}\text{P}(\text{Im})(\text{O}_2)$ , and  $\text{Fe}^{\text{II}}\text{P}(\text{CO})$ . In the first two cases, DFT calculations fail to predict the high-spin nature of the system. The other two are examples of low-spin hemes whose electronic and geometrical properties are, in principle, correctly captured by standard density-functional simulations. These four case studies were chosen for their respective relevance in bioinorganic chemistry, and to illustrate the performance of the DFT+U method on heme models exhibiting a variety of coordination modes and multiplicities.

#### A. Five coordinated heme-imidazole complex

The  $\text{Fe}^{\text{II}}\text{P}(\text{Im})$  system, depicted in Fig. 2, has been the target of numerous computational studies, inasmuch as it appears as the natural model to represent the unbound active site of several heme proteins, in particular hemoglobin and myoglobin.<sup>7,13–15,32</sup> As mentioned above, the ground state of this compound has been experimentally characterized as a quintuplet ( $S=2$ ), whereas DFT calculations yield a triplet ground state ( $S=1$ ). In Table II the energetic separations between the low lying spin states resulting from DFT and DFT+U are compared.

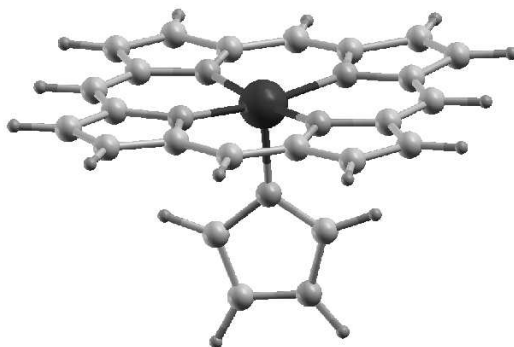


FIG. 2: Structure of the five coordinated  $\text{Fe}^{\text{II}}\text{P}(\text{Im})$  complex.

According to PBE, the triplet is around 8 kcal/mol more stable than the quintuplet or the singlet; similar gaps are obtained with the BP86 exchange-correlation functional.<sup>13</sup> On the other hand, the transition energy between the triplet and the quintuplet is reduced to nearly 2 kcal/mol if B3LYP is used.<sup>14</sup> As previously noted, the introduction of the HF exchange in the DFT functional stabilizes high multiplicity states, but in this case B3LYP is still unable to provide the right splittings.

The formalism summarized in equation (6) gives for this system a  $U_{sc}$  of 3.9 eV and a  $U'_{sc}$  of 2.5 eV (Fig. 3). If any of these values are adopted, DFT+U restores the experimental ordering of the spin states. The total energies of the low lying states as a function of  $U$  are depicted in Fig. 4. The increase of the  $U$  parameter equalizes the triplet and the quintuplet energies, producing a spin crossover at  $U \approx 2$  eV. At higher values of  $U$ , the quintuplet remains the ground state.

Fig. 5 highlights the effect of  $U$  on the electronic symmetry of the d states in the heme porphyrin. Spin occupations were computed by projecting the electronic wavefunctions on the atomic orbitals of the iron, as prescribed by equation (3). The upper panel of Fig. 5 represents the occupations of the minority spin manifold in the quintuplet state. Iron(II) is a

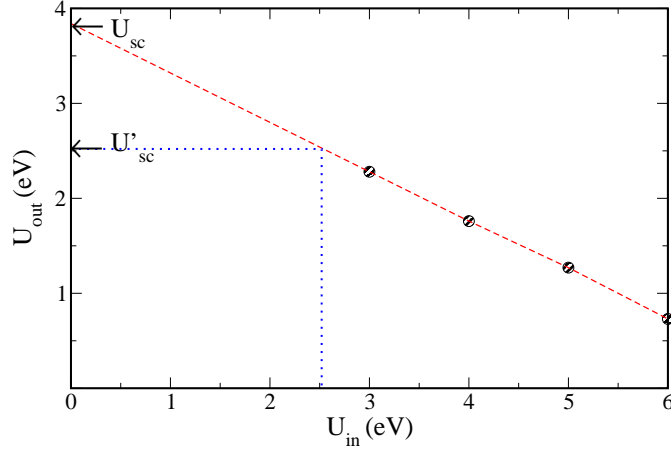


FIG. 3: Linear response calculation of the  $U$  parameter on the quintuplet state of the  $\text{Fe}^{\text{II}}\text{P}(\text{Im})$  complex.

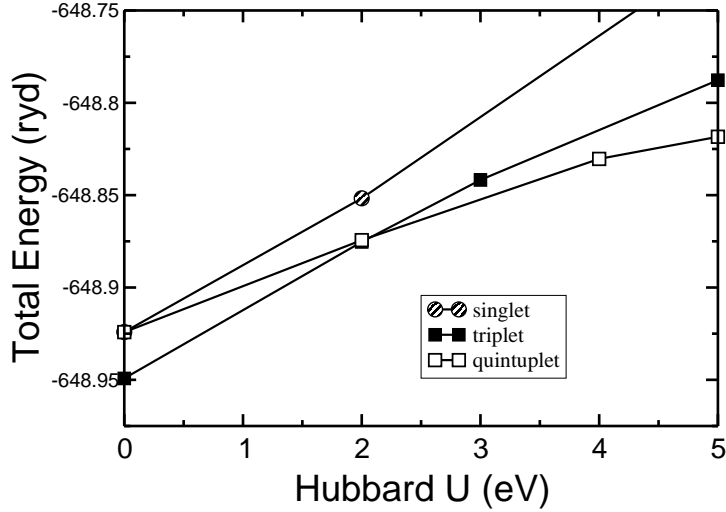


FIG. 4: Total energy of the low lying spin states of the  $\text{Fe}^{\text{II}}\text{P}(\text{Im})$  complex as a function of the  $U$  parameter.

$d^6$  ion and the quintuplet bears four unpaired electrons, therefore the sum of the occupations on the minority spin channel should be around 1. It is not exactly 1 because the eigenstates of the complex do not correspond to pure  $d$  atomic orbitals, but are instead strongly hybridized. Yet, it is possible to assign the electronic configuration of the system in terms of  $d$  atomic

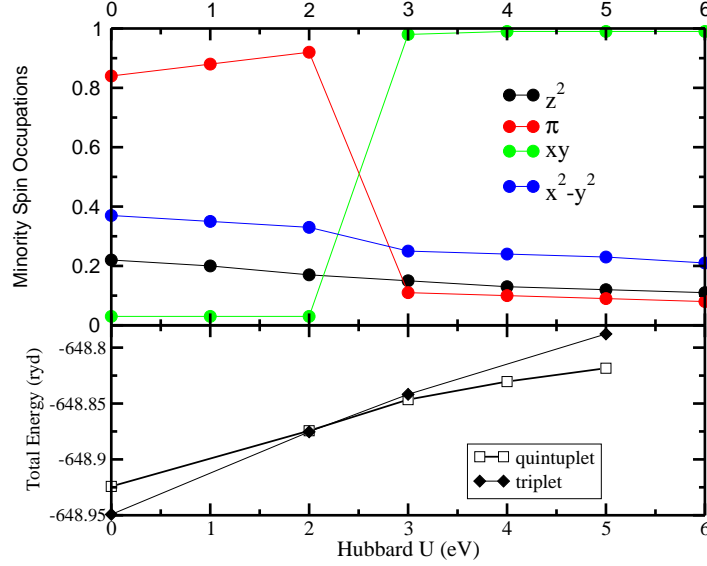


FIG. 5: Occupations of the minority spin manifold in the quintuplet state of the  $\text{Fe}^{\text{II}}\text{P}(\text{Im})$  complex.

The lower panel shows the total energy of the two lowest accessible spin states as a function of  $U$ .

orbitals, depending on whether the occupations are close to 0 or 1. Note that by convention, the nitrogen atoms of the porphyrin ring are placed on the  $xy$  plane, with the  $x$  and  $y$  axes oriented along the Fe-N bonds. Pure DFT ( $U=0$ ), and DFT+ $U$  with  $U < 2$  eV, converge to the  $(d_{z^2})^1 (d_{xy})^1 (d_{\pi})^3 (d_{x^2-y^2})^1$  state.<sup>33</sup> This is the same configuration as reported by Spiro and coworkers from B3LYP simulations.<sup>14</sup> The increase of  $U$  above 2 eV stabilizes the  $(d_{z^2})^1 (d_{xy})^2 (d_{\pi})^2 (d_{x^2-y^2})^1$  state, which is the one experimentally assigned to  $\text{Fe}^{\text{II}}\text{P}(\text{Im})$ .<sup>6</sup> Interestingly enough, this change in configuration is associated with an inversion in the relative energy of the triplet and the quintuplet, which now becomes the ground state.

The examination of the optimized geometry at a finite  $U$  of 3.9 eV shows an agreement with the experimental data at least as good as pure DFT does. The structural parameters most affected by the  $U$  correction are those in the vicinity of the metal center, presented in Table III. The out-of-plane displacement of the iron,  $d_{\text{Fe}-p}$ , is the distance of the iron to the average plane defined by the four nitrogen atoms of the porphyrin ring. The interplay

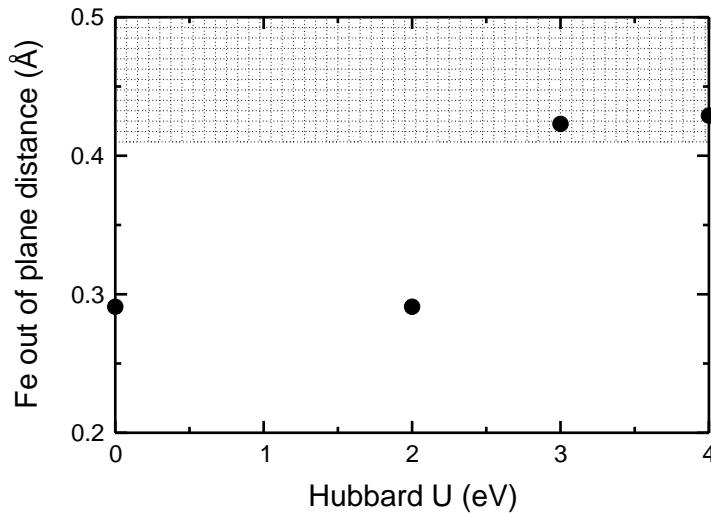


FIG. 6: Distance of the iron to the average plane defined by the four nitrogen atoms of the porphyrin ring as a function of  $U$  in  $\text{Fe}^{\text{II}}\text{P}(\text{Im})$ . The shaded area encompasses the experimental region.

between spin state and  $d_{\text{Fe}-p}$ , often involved in the dynamics of the heme protein—as for example in the allosteric mechanism of hemoglobin<sup>34</sup>—has been characterized experimentally<sup>6</sup> and theoretically.<sup>13,14</sup> Table III contrast this and other optimized structural parameters with the experimental data available for the synthetic model compound  $\text{Fe}^{\text{II}}\text{TPP}(2\text{-MeIm})$  (TPP: tetraphenyl porphine; 2-MeIm: 2-methyl imidazole).<sup>35</sup> Fig. 6 shows the dependence of  $d_{\text{Fe}-p}$  on  $U$ , with the shaded part of the graph indicating the experimental region.

In summary: the  $U$  term favors the stabilization of the  $(d_{xy})^2$  configuration—deemed the experimental ground state of the complex—rendering this (quintuplet) state the lowest in energy, as can be seen in the lower panel of Fig. 5.

### B. Iron(III) porphyrinato chloride

The low lying accessible electronic states for the penta-coordinate  $\text{Fe}^{\text{III}}\text{P}(\text{Cl})$  complex, with five d-electrons, are the sextet, the quartet, and the doublet ( $S=5/2$ ,  $S=3/2$  and  $S=1/2$ ,

respectively). Similarly to the situation discussed in the previous section, DFT can not reproduce the high spin character of the system, which has been established experimentally.<sup>36</sup> Using a battery of ab-initio methods, Ghosh and collaborators have explored this complex in depth.<sup>8,37,38</sup> They found that, while the PW91 exchange-correlation functional yields a quartet state 8.1 kcal/mol more stable than the sextet, B3LYP provides nearly identical energies for both configurations. Higher-level CASPT2 calculations and CCSD(T) simulations on a smaller model system are consistent with experiments, placing the sextet almost 20 kcal/mol below the quartet.<sup>37,38</sup> These results are summarized in Table IV.

Fig. 7 shows that, as seen in  $\text{Fe}^{\text{II}}\text{P}(\text{Im})$ , the  $U$  term stabilizes the highest multiplet in  $\text{Fe}^{\text{III}}\text{P}(\text{Cl})$ . A spin inversion is verified at  $U \approx 1.5$  eV, rendering the sextet as the ground state. A value of  $U_{sc}$  equal to 4.0 eV is obtained, which leads to a sextet-quartet transition energy of 9.2 kcal/mol. Table IV makes evident the poor performance of density-functionals to describe multiplet splittings in transition metals, capable of errors in the order of tens of kcal/mol. Despite its quantitative disagreement with the highly correlated methods (whose ultimate accuracy is, on the other hand, difficult to assess in this case), DFT+U succeeds in recovering the ordering of the spin states.

### C. Six coordinated oxyheme model

The  $\text{Fe}^{\text{II}}\text{P}(\text{Im})(\text{O}_2)$  system has been long identified as low spin in native proteins and in synthetic compounds.<sup>6</sup> Its importance as the oxygenated model of hemoglobin and myoglobin is reflected in the literature, which—aside from the experimental work—offers many computational studies addressing the electronic and structural aspects of the complex.<sup>13,32,39</sup> The low spin nature of six coordinated iron porphyrins is in general correctly described by DFT, consequently with its trend to unstabilize high multiplicity states. In the particular

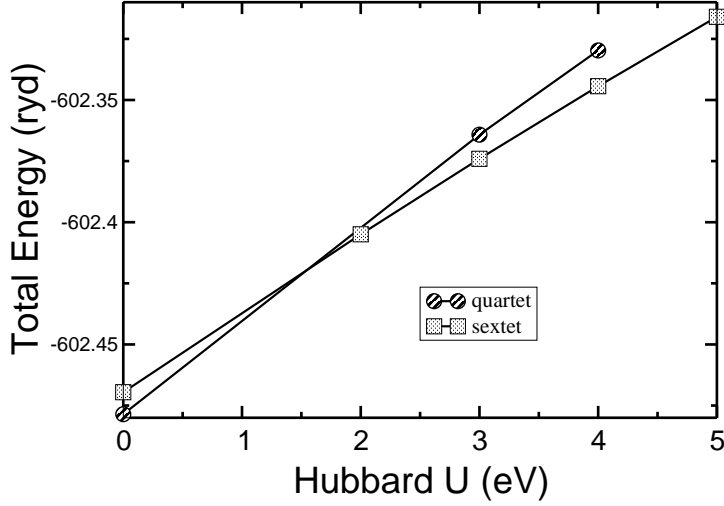


FIG. 7: Total energy of the lowest accessible spin states of the  $\text{Fe}^{\text{II}}\text{P}(\text{Cl})$  complex as a function of the  $U$  parameter.

case of  $\text{Fe}^{\text{II}}\text{P}(\text{Im})(\text{O}_2)$ , calculations with different functionals, including B3LYP, indicate a singlet ground state of open-shell character.<sup>7,13</sup> While the total spin of the molecule is zero, DFT calculations reveal partial spin densities localized on the d orbitals of Fe and the  $\pi^*$  orbitals of  $\text{O}_2$ , integrating approximately to +1 and -1, corresponding to two unpaired electrons of opposite spin.<sup>7,13</sup> This open-shell singlet (o.s.s.) state can be interpreted as the result of an antiferromagnetic coupling between  $\text{Fe}^{\text{II}}\text{P}(\text{Im})$  ( $S=2$ ) and  $\text{O}_2$  ( $S=1$ ), each retaining part of its magnetic character upon binding.

DFT+U supports this picture: Fig. 8 depicts the spin density,  $\rho_{\text{spin}}(\mathbf{r}) = \rho_{\alpha}(\mathbf{r}) - \rho_{\beta}(\mathbf{r})$ , computed at a finite  $U$  of 4 eV. This figure is qualitatively equivalent to the one reported by Rovira and coworkers using pure DFT.<sup>13</sup> The impact of the  $U$  parameter on the total energies of the lowest accessible spin states is plotted in Fig. 9. The progressive increment of  $U$  further stabilizes the o.s.s. with respect to the closed-shell singlet and the triplet. On the other hand, the gap between the o.s.s. and the quintuplet is reduced, but the raise



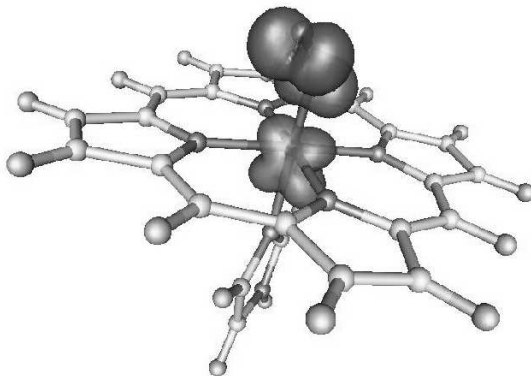


FIG. 8: Spin density in  $\text{Fe}^{\text{II}}\text{P}(\text{Im})(\text{O}_2)$  corresponding to an open-shell singlet, calculated with DFT+U. Lobes localized on the iron and on the  $\text{O}_2$  represent unpaired electron density of opposite spin.

in  $U$  beyond 4 eV produces the dissociation of the Fe-O bond in the o.s.s. before a spin crossing between these two states is observed. The effect of the on-site correction can also be examined through the absolute magnetization of the molecule, defined as  $\int |\rho_\alpha(\mathbf{r}) - \rho_\beta(\mathbf{r})| d\mathbf{r}$ , a measure of the unpaired electron density in the system. Fig. 10 illustrates how the on-site correlation affects the distribution of the unpaired electron density, reinforcing, in particular, the antiferromagnetic character of the o.s.s. The net effect of  $U$  is seemingly to thwart the coupling of the unpaired electrons of the molecular oxygen and the porphyrin, stabilizing the separate species, which is reflected in the elongation of the Fe-O distance discussed below. The absolute magnetization augments from 1.8 at  $U=0$  to 3.2 at  $U=4$  eV, a value placed halfway from that corresponding to the unbound system, comprised of a triplet plus a quintuplet ( $S=1+2$ ).

Extrapolation to the  $y$ -axis in the  $U_{in} - U_{out}$  plot (Fig. 11) yields a  $U_{sc}$  of 5.9 eV, sensibly higher than in the previous examples. This value induces the rupture of the Fe-O bond, and

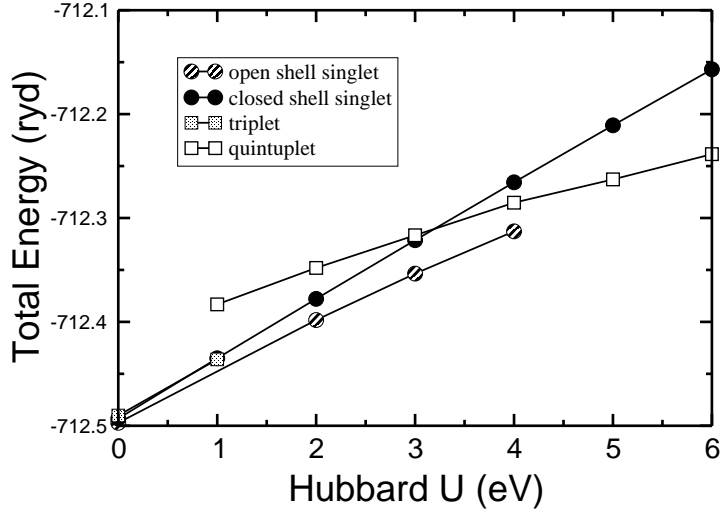


FIG. 9: Total energy of the low lying spin states of  $\text{Fe}^{\text{II}}\text{P}(\text{Im})(\text{O}_2)$  as a function of the  $U$  parameter.

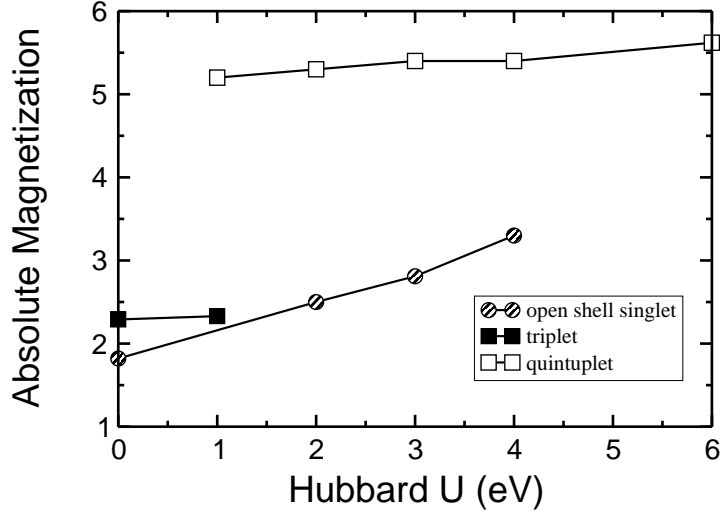


FIG. 10: Absolute magnetization of the low lying spin states of  $\text{Fe}^{\text{II}}\text{P}(\text{Im})(\text{O}_2)$  as a function of the  $U$  parameter.

in consequence it is not possible to obtain a relaxed, bound complex associated with this  $U_{sc}$ . As seen in Fig. 12, where the Fe-O distance is plotted as a function of  $U$ , the increase in the on-site correction provokes the elongation of the bond, eventually leading to the dissociation of the complex. The shaded area in the graph encloses the range of experimental Fe-O

lengths observed in different model compounds. It is important to emphasize that such values correspond to synthetic or natural compounds in which the  $O_2$  molecule is stabilized in the axial position by virtue of a second interaction on the distal side, namely an hydrogen bond or some kind of trapping or cage effect. In the absence of a distal cavity, oxygenation of iron (II) porphyrins under ordinary conditions has been rarely observed.<sup>40,41</sup> Pure DFT and B3LYP systematically overestimate the binding of  $O_2$ , giving for the free heme energies in the range of 15-25 kcal/mol,<sup>13,32</sup> in direct contradiction with the experimental difficulty to isolate the oxygenated species. While part of this error is associated with the underestimation of the total energy of the quintuplet, such overbinding represents a major problem in the application of DFT to the calculation of affinity constants. Fig. 13 shows that DFT+U provides a more realistic oxygen affinity, the binding energy decreasing from 28 kcal/mol at  $U=0$  to around 1 kcal/mol at  $U=4$  eV. In the present case,  $U'_{sc}$  turns out to be 1 eV lower than  $U_{sc}$  (Fig. 11). A  $U$  of 5.8 eV, as obtained from equation (6), is too high to represent the thermodynamic and geometrical properties of the oxygenated complex. This is evincing a positive bias in the linear response approach, which will be manifested also in other low spin systems. We will come back to this issue later in the next sections.

#### **D. Five coordinated carboxyheme model**

As the last case study, we will briefly discuss the  $Fe^{II}P(CO)$  complex. Five and six coordinated carboxyhemes are low spin systems whose electronic and geometrical features are well reproduced by DFT, notwithstanding the overestimation of the CO binding energy, similarly to what is found with  $O_2$ . The motivation to include the carboxylated complex in this study is therefore to assess the behavior of DFT+U in comparison with standard density-functional theory, in particular to examine if the former produces any detrimental bias in a

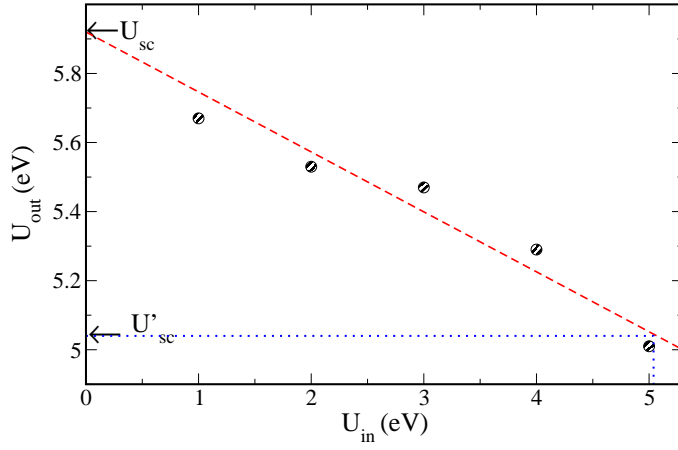


FIG. 11: Linear response calculation of the  $U$  parameter on the open-shell singlet state of the  $\text{Fe}^{\text{II}}\text{P}(\text{Im})(\text{O}_2)$  complex.

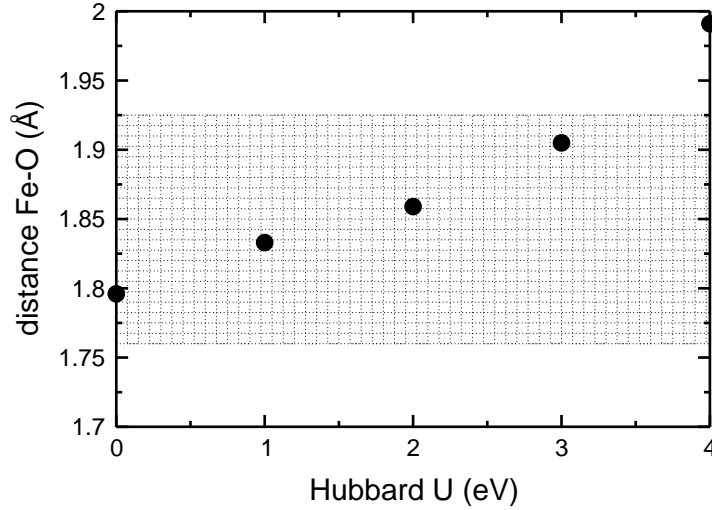


FIG. 12: Fe-O bond length as a function of the  $U$  parameter in  $\text{Fe}^{\text{II}}\text{P}(\text{Im})(\text{O}_2)$ . The shaded area encompasses the experimental region.

case where the latter shows already a good performance. Table V contains computed and experimental values for a few selected properties of the carboxyheme. The general agreement between the simulations and the X-ray data is benefited from the  $U$  term, which not only provides a marginal improvement on the geometrical parameters of the complex, but also

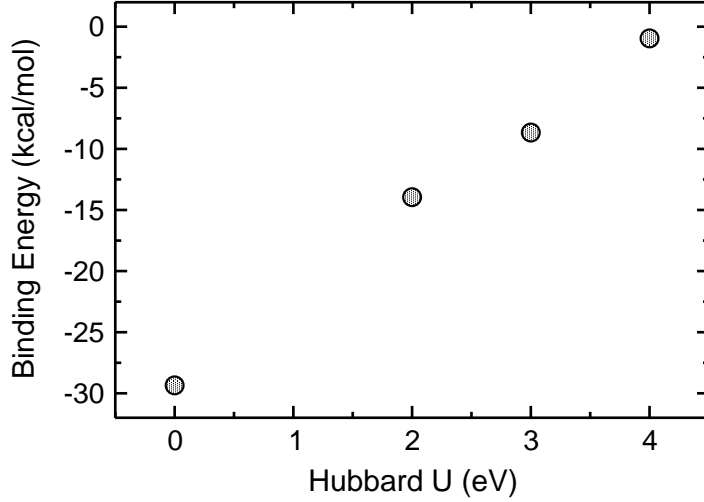


FIG. 13: Energy of  $\text{O}_2$  binding to  $\text{Fe}^{\text{II}}\text{P}(\text{Im})$  as a function of the  $U$  parameter.

corrects for the overbinding trend exhibited by pure DFT. At the same time, however, the enhancement of the on-site correlations closes the gap between the singlet and the quintuplet, to the extent that for  $U \geq 4$  eV the latter becomes the most stable state (Fig. 14).

The response of the system to the change in orbital occupations resembles the case of  $\text{Fe}^{\text{II}}\text{P}(\text{Im})(\text{O}_2)$ , yielding for  $U_{sc}$  and  $U'_{sc}$  values of 7.2 and 5.3 eV respectively (Fig. 15). Since neither experimental, nor reliable theoretical estimations of the spin transition energies are available, we can not evaluate the magnitude of the error in the self-consistent  $U$  obtained with each criteria. In principle, only values below 4 eV are consistent with the experimental singlet state, and so it is evident that both  $U_{sc}$  and  $U'_{sc}$  suffer from some overestimation. Interestingly enough, the self-consistent  $U$  parameter calculated in a high spin configuration of the carboxyheme turns out to be significantly smaller, as depicted also in Fig. 15. On the other hand, linear response calculations on the low spin state of the  $\text{Fe}^{\text{II}}\text{P}(\text{Im})$  system return values of  $U_{sc}$  above 6 eV (data not shown). This is indicating that the response of the system depends more on the multiplicity than on the particular geometry, coordination

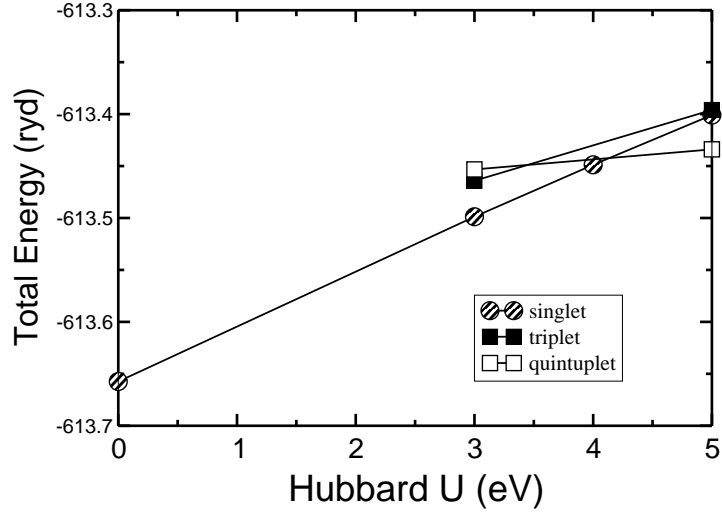


FIG. 14: Total energy of the low lying spin states of Fe<sup>II</sup>P(CO) as a function of the  $U$  parameter.

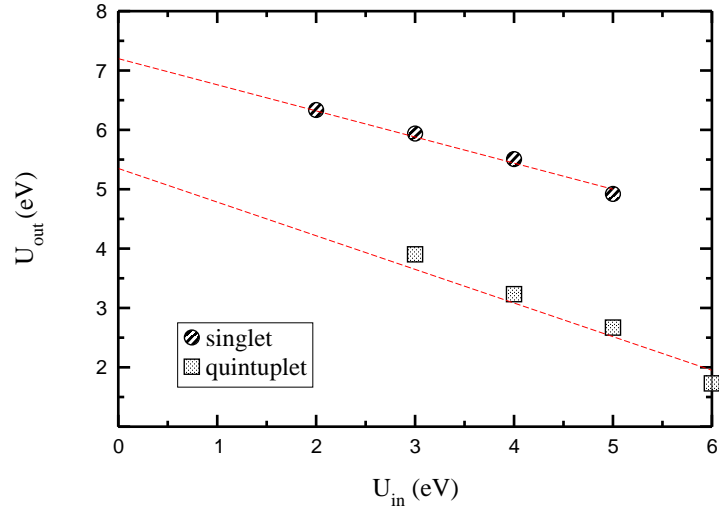


FIG. 15: Linear response calculation of the  $U$  parameter on the singlet and quintuplet states of the Fe<sup>II</sup>P(CO) complex.

mode, or the nature of the ligands.

#### IV. CONCLUSIONS AND FINAL REMARKS

The inclusion of on-site correlations via a Hubbard term in DFT rectifies the trend of density-functionals to overstabilize low spin states in iron porphyrins. At variance with DFT, with Hartree-Fock, and with hybrid methods, which successfully describe some of the possible coordination modes of the complex but fail in the rest,<sup>7</sup> DFT+U is capable to provide the qualitatively correct splittings in low and high spin iron porphyrins at the same time, if the proper parameter is adopted. This improvement is also reflected in the geometry optimizations, and, more importantly, in more realistic binding energies to diatomic ligands. The question of whether a hybrid functional with the proper exchange and correlation contributions would be capable to recover the spin state energetics of the full iron porphyrins series is still open. We have addressed this question in a previous article,<sup>7</sup> with no positive results. In our experience, the combination of the HF exchange with the GGA exchange-correlation leads to hybrid methods reflecting either the behavior of pure DFT—overstabilizing low spin states—or the behavior of Hartree-Fock—favoring high spin states. To the best of our knowledge, no hybrid has been reported that retains the best of both approaches in the description of iron porphyrins, but a more extensive search is probably needed before giving a definite answer.

The application of the linear response calculation to low spin states leads to self-consistent Hubbard parameters 1 or 2 eV above the optimal ones. The linear response of the system appears to be more dependent on the spin state than on the coordination number or the identity of the ligands. In fact, plots of  $U_{in}$  versus  $U_{out}$  belonging to different complexes in the same spin state exhibit a high similarity. The reason for the overestimation of the Hubbard  $U$  in low spin configurations is not evident. Different extensions to the linear

response approach were explored, including the partition of  $U$  into  $U^\alpha$  and  $U^\beta$  to discriminate between both spin channels, and even between the five d states. Additionally, a  $J$  term to represent separately the on-site exchange was implemented. The modifications described above, however, produced little or no effect on the resulting  $U_{sc}$ . The investigation of other factors which could be responsible for these biases is in progress. In any case, values of  $U$  of 4 eV or slightly lower seem the optimal to reproduce the electronic, thermodynamic and structural properties of the heme compounds.

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- <sup>1</sup> Collman, J. P.; Hoard, J. L.; Kim, N.; Lang, G.; Reed, C. A. *J. Am. Chem. Soc.*, **1975**, 97, 2676.
- <sup>2</sup> Lang, G.; Spartalian, K.; Reed, C. A.; Collman, J. P. *J. Chem. Phys.*, **1978**, 69, 5424.
- <sup>3</sup> Boyd, P. D. W.; Buckingham, A. D.; McMecking, R. M.; Mitra, S. *Inorg. Chem.*, **1979**, 18, 3585.
- <sup>4</sup> Goff, H.; La Mar, G. N.; Reed, C. A. *J. Am. Chem. Soc.*, **1977**, 99, 3641.
- <sup>5</sup> Mispelter, J.; Momenteau, M.; Lhoste, J. M. *J. Chem. Phys.*, **1980**, 72, 1003.
- <sup>6</sup> Scheidt, W. R.; Reed, C. A. *Chem. Rev.*, **1981**, 81, 543.
- <sup>7</sup> Scherlis, D. A.; Estrin, D. A. *Int. J. Quantum Chem.*, **2002**, 87, 158.
- <sup>8</sup> Ghosh, A.; Taylor, P. R. *Curr. Opin. Chem. Biol.*, **2003**, 7, 113.
- <sup>9</sup> Ghosh, A.; Taylor, P. R. *J. Chem. Theory Comput.*, **2005**, 1, 597.
- <sup>10</sup> Deeth, R. J.; Fey, N. *J. Comput. Chem.*, **2004**, 25, 1840.
- <sup>11</sup> Smith, D. M. A.; Dupuis, M.; Straatsma, T. P. *Mol. Phys.*, **2005**, 103, 273.
- <sup>12</sup> Harvey, J. N. *Struct. Bonding*, **2004**, 112, 151.
- <sup>13</sup> Rovira, C.; Kunc, K.; Hutter, J.; Ballone, P.; Parrinello, M. *J. Phys. Chem. A*, **1997**, 101, 8914.
- <sup>14</sup> Kozlowski, P. M.; Spiro, T. G.; Zgierski, M. Z. *J. Phys. Chem. B*, **2000**, 104, 10659.
- <sup>15</sup> Liao, M.-S.; Scheiner, S. *J. Chem. Phys.*, **2002**, 116, 3635.
- <sup>16</sup> Choe, Y.-K.; Nakajima, T.; Hirao, K.; Lindh, R. *J. Chem. Phys.* **1999**, 111, 3837.
- <sup>17</sup> A <sup>3</sup>B state turns out to be 0.12 eV more stable than the lowest singlet state. See Jensen, K. P.; Roos, B. O.; Ryde, U. *J. Inorg. Biochem.* **2005**, 99, 45.
- <sup>18</sup> Anisimov, V. I.; Zaanen, J.; Andersen, O. K. *Phys. Rev. B* **1991**, 44, 943.

- <sup>19</sup> Anisimov, V. I.; Solovyev, I. V.; Korotin, M. A.; Czyzyk, M. T.; Sawatzky, G. A. *Phys. Rev. B* **1993**, 48, 16929.
- <sup>20</sup> Solovyev, I. V.; Dederichs, P. H.; Anisimov, V. I. *Phys. Rev. B* **1994**, 50, 16861.
- <sup>21</sup> Liechtenstein, A. I.; Anisimov, V. I.; Zaanen, J. *Phys. Rev. B* **1995**, 52, R5467.
- <sup>22</sup> Dudarev, S. L.; Botton, G. A.; Savrasov, S. Y.; Humphreys, C. J.; Sutton, A. P. *Phys. Rev. B* **1998**, 57, 1505.
- <sup>23</sup> Kulik, H. J.; Cococcioni, M.; Scherlis, D. A.; Marzari, N. *Phys. Rev. Lett.* **2006**, 97, 103001.
- <sup>24</sup> Rollmann, G.; Herper, H. C.; Entel, P. *J. Phys. Chem. A* **2006**, 110, 10799.
- <sup>25</sup> Leung, K.; Rempe, S. B.; Schultz, P. A.; Sproviero, E. M.; Batista, V. S.; Chandross, M. E.; Medforth, C. J. *J. Am. Chem. Soc.* **2006**, 128, 3659.
- <sup>26</sup> Nolan, M.; Parker, S. C.; Watson, G. W. *J. Phys. Chem. B* **2006**, 110, 2256.
- <sup>27</sup> Nolan, M.; Watson, G. W. *J. Phys. Chem. B* **2006**, 110, 16600.
- <sup>28</sup> Baroni, S.; Dal Corso, A.; de Gironcoli, S.; Giannozzi, P.; Cavazzoni, C.; Ballabio, G.; Scandolo, S.; Chiarotti, G.; Focher, P.; Pasquarello, A.; Laasonen, K.; Trave, A.; Car, R.; Marzari, N.; Kokalj, A. <http://www.quantum-espresso.org/>.
- <sup>29</sup> Perdew, J. P.; Burke, K.; Ernzerhof, M. *Phys. Rev. Lett.* **1996**, 77, 3865.
- <sup>30</sup> Vanderbilt, D. *Phys. Rev. B* **1990**, 41, 7892.
- <sup>31</sup> Cococcioni, M.; de Gironcoli, S.; *Phys. Rev. B*, **2005**, 71, 35105.
- <sup>32</sup> Marti, M. A.; Crespo, A.; Capece, L.; Boechi, L.; Bikiel, D. E.; Scherlis, D. A.; Estrin, D. A. *J. Inorg. Biochem.* **2006**, 100, 761.
- <sup>33</sup> We denote by  $d_\pi$  the linear combinations  $d_{xz} \pm d_{yz}$ , so  $d_\pi$  can be occupied by up to four electrons.
- <sup>34</sup> Strayer, L. *Biochemistry*, 4th ed.; W. H. Freeman and Company: New York, 1995.
- <sup>35</sup> Hoard, J. L. In *Porphyrins and Metalloporphyrins*; K. M. Smith Ed.; Elsevier: Amsterdam,

New York, 1975.

- <sup>36</sup> Reed, C. A.; Guiset, F. *J. Am. Chem. Soc.* **1996**, 118, 3281.
- <sup>37</sup> Ghosh, A.; Persson, B. J.; Taylor, P. R. *J. Biol. Inorg. Chem.* **2003**, 8, 507.
- <sup>38</sup> Ghosh, A.; Gonzalez, E.; Vangberg, T.; Taylor, P. *J. Porphyrins Phthalocyanines* **2001**, 5, 345.
- <sup>39</sup> Scherlis, D. A.; Estrin, D. A. *J. Am. Chem. Soc.* **2001**, 123, 8436.
- <sup>40</sup> Momenteau, M.; Reed, C. A. *Chem. Rev.* **1994**, 94, 659.
- <sup>41</sup> Oertling, W. A.; Kean, R. T.; Wever, R.; Babcock, G. T. *Inorg. Chem.* **1990**, 29, 2633.
- <sup>42</sup> Peng, S.-M.; Ibers, J. A. *J. Am. Chem. Soc.* **1976**, 98, 8032.

TABLE I: Experimental and calculated electronic ground states of five and six coordinated iron porphines (FeP), with the following axial ligands: O<sub>2</sub>, CO, imidazole (Im), and chloride.

	Six coordinated		Five coordinated		
	FeP(Im)(O <sub>2</sub> )	FeP(Im)(CO)	FeP(CO)	FeP(Im)	FeP(Cl)
Experimental	singlet	singlet	singlet	quintuplet	sextet
Hartree-Fock	quintuplet	quintuplet	quintuplet	quintuplet	sextet
DFT-GGA	singlet	singlet	singlet	triplet	quartet
B3LYP	singlet	singlet	singlet	triplet	quartet/sextet

TABLE II: Spin transition energies (kcal/mol) for the low lying spin states of Fe<sup>II</sup>P(Im) calculated with several density-functionals and with DFT+U, using  $U_{sc}$ =3.9 eV.

		Singlet	Triplet	Quintuplet
DFT	PBE <sup>a</sup>	7.8	0.0	7.9
	BP86 <sup>b</sup>	8.3	0.0	6.5
	B3LYP <sup>c</sup>	5.8	0.0	1.9
DFT+U		20.9	4.9	0.0

<sup>a</sup>Pseudopotential calculations with plane wave basis set. <sup>b</sup>Pseudopotential calculations with plane wave basis set, from ref.<sup>13</sup>. <sup>c</sup>Gaussian calculations (VTZ basis), from ref.<sup>14</sup>.

TABLE III: Selected experimental and optimized structural parameters ( $\text{\AA}$ ) in  $\text{Fe}^{\text{II}}\text{P}(\text{Im})$ .

	$d_{\text{Fe}-p}$	$\text{Fe-N}_{\text{porph}}$	$\text{Fe-N}_{\text{imi}}$
Experimental <sup>a</sup>	0.42	2.09	2.16
DFT (PBE)	0.29	2.07	2.13
DFT+U ( $U_{sc}=3.9$ eV)	0.43	2.11	2.19

<sup>a</sup>Data for  $\text{Fe}^{\text{II}}\text{TPP}(2\text{Me-Im})$  from ref.<sup>35</sup>.

TABLE IV: Spin transition energies (kcal/mol) for the low lying spin states of  $\text{Fe}^{\text{II}}\text{P}(\text{Cl})$  calculated with highly correlated methods and density functional theory, including DFT+U ( $U_{sc}=4.0$  eV).

	Quartet	Sextet
CASPT2 <sup>a</sup>	19.6	0.0
RCCSD(T) <sup>b</sup>	16.1	0.0
DFT-PBE	0.0	5.6
DFT-PW91 <sup>c</sup>	0.0	8.1
DFT+U	9.2	0.0

<sup>a</sup>Ref.<sup>37</sup>. <sup>b</sup>Calculations on a simplified model, ref.<sup>38</sup>. <sup>c</sup>Ref.<sup>37</sup>.

TABLE V: Selected bond distances ( $\text{\AA}$ ) and CO binding energy (kcal/mol) for the  $\text{Fe}^{\text{II}}\text{P}(\text{CO})$  complex calculated with DFT+U.

U (eV)	Fe-C(CO)	Fe-N <sub>porph</sub>	C-O	$\Delta E$
0.0	1.69	1.99	1.17	-45.3
3.0	1.71	2.00	1.16	-26.1
5.0	1.74	2.01	1.16	-12.0
Experimental <sup>a</sup>	1.77	2.02	1.12	-

<sup>a</sup>The experimental model is axially coordinated to pyridine, ref.<sup>42</sup>.